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Workshop on the Benefits of Reductions in Exposure to Hazardous Air Pollutants: Developing Best Estimates of Dose-Response Functions

An SAB Workshop Report of an EPA/SAB Workshop

NOTICE

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TABLE OF CONTENTS

1. BACKGROUND

Hazardous Air Pollutants (HAPs) include pollutants identified in the Clean Air Act; pollutants known to cause or suspected of causing cancer or other serious human health effects, such as birth defects, neurological damage, and respiratory disease.[1] While it is clear that reducing emissions of HAPs to the atmosphere will reduce exposure levels to chemical agents that can cause serious health problems, there is no scientific consensus on the best way to quantify such risk reductions for the purpose of a benefits analysis. Nor is there consensus on how to value the reductions in risk, or what risk measures will be needed for valuation. The goal of this workshop was to consider improvements to methods for estimating changes in health risks resulting from regulations of HAPs that can be combined with valuation functions to estimate monetized benefits of HAP reductions. Improved methods for assessing HAPs benefits will assist the Agency in analyzing the economic value of its programs and in preparing reports to Congress, such as analyses of the benefits and costs of the Clean Air Act (CAA), as required by Section 812 of the CAA.

The workshop responded to a recommendation from the Health and Ecological Effects Subcommittee of the Advisory Council on Clean Air Compliance Analysis in 1999. Members and consultants from the Science Advisory Board (SAB) served individually on a committee with Agency staff to plan the workshop, where Agency staff, SAB members and consultants, experts outside the Board, and the public explored possible new methods for monetizing HAPs benefits. EPA explicitly sought a broad spectrum of views at the workshop and did not seek a consensus recommendation from workshop participants.

The workshop brought together expert discussants in the fields of economics, health science, and risk assessment as related to managing HAPs, with the help of the workshop chair and moderator, Dr. Michael Kleinman, College of Medicine, University of California, Irvine, California. The workshop took a "case study" approach to address two main issues:

a) Whether it is possible to produce best estimates of the central tendencies and distributions of the dose-response functions for a set of well-defined health endpoints for each of the case-study HAPs for use in the future activities on air quality and exposure modeling and how that might best be done.

b) How best to identify limitations and uncertainties in both risk assessment methods and economic models with regard to changes in health risks from reductions in air toxic emissions.

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[1] Section 112(b) of the Clean Air Act describes hazardous air pollutants as those pollutants "which present, or may present, through inhalation or other routes of exposure, a threat of adverse human health effects (including, but not limited to, substances which are known to be, or may reasonably be anticipated to be, carcinogenic, mutagenic, teratogenic, neurotoxic, which cause reproductive dysfunction, or which are acutely or chronically toxic) or adverse environmental effects"

Details about the workshop process, a list of participants and agenda can be found in Appendices A-B.

The centerpiece of the workshop was a dialogue between economists and risk assessors. Dr. Lester Lave, an economist from Carnegie-Mellon University, set the stage with a white paper that documented his view of what benefits assessors need to know; why current toxicological information is not suited to provide this information; and a research agenda that would improve this estimation.

In response to his challenge, three distinguished experts prepared white paper case studies (see Appendix F). Examining chemicals for which there are substantial databases on health effects and exposure, the case studies were designed to illustrate the diversity of situations among various HAPs:

a) Benzene: a case with substantial data on cancer and non-cancer effects and strong hazard identification.[2] Case presented by Dr. Bernard Goldstein, Environmental and Occupational Health Sciences Institute, Robert Wood Johnson School of Medicine.

b) Perchloroethylene: a case with substantial, but not as consistent, data on cancer and data on noncancer hazards.[3] Case presented by Dr. Lorenz Rhomberg, Gradient Corporation.

c) Manganese: a case of a neurotoxin that causes many structural and functional effects, including a condition similar to Parkinson's Disease, and whose effects may accelerate the process of aging or onset of disease, albeit perhaps significantly after exposure.[4] Case presented by Dr. Bernard Weiss, University of Rochester.

The White Papers can be found on the SAB website (www.epa.gov/sab) as Appendix F of this Workshop Report.

These presentations were followed by a discussion where expert panelists (three

[2] Although the first case (Benzene), exemplified a HAP for which there is substantial epidemiological and toxicological evidence, it also highlighted some common areas of uncertainty in HAP risk assessments: extrapolation from health effect observations at higher exposures to assessment of lower exposure scenarios (e.g., uncertainties regarding carcinogenesis and the shape of the cancer dose response curve at low exposures); issue of "background" levels; cumulative burden; and other exposure-related issues.

[3] The second white paper (Perchloroethylene) highlighted additional issues and raised the possibility that the conclusions drawn from toxicological databases may lead us to conflicting or inconclusive results. Specifically, uncertainties in extrapolating health effect observations from laboratory animals to humans were highlighted.

[4] The third paper (Manganese) explored a very different terrain. In this case, the author created a conceptual model highlighting the idea that specific studied endpoints may be markers for a broader set of conditions and that the challenge for economists may be valuing a shift in the onset of risk or in the risk profile/trajectory of a population over their lifetime (after perhaps a long latency period).

economists and three health scientists) each were asked to address the two central workshop questions and reflect on the approaches proposed in the three chemical-specific white papers. Most of the expert panelists, and the Workshop Co-Moderator, Dr. Roy Albert, expanded on their brief presentations in written comments submitted after the workshop. These written submissions can be found on the SAB website (www.epa.gov/sab) as Appendix G of this Workshop Report.

2. MAJOR THEMES

The three white papers and remarks by Dr. Lester Lave generated lively discussion but no consensus on a proposed methodology. Many specific options emerged in the discussion and in panelists' written comments. Appendix F lists many of the different strategies suggested for bridging the gaps. There was, however, general agreement that this was a fertile area for further study and that there was a need for further cross-disciplinary work between risk assessors and economists/analysts.

During the workshop discussion, it was noted that the different disciplines are pursuing fundamentally different questions. In general, regulatory toxicologists are asking, "What level is likely to be safe?" Economists, on the other hand, are asking, "What are the number of cases reduced per small unit change in pollution concentration from individual regulations?" Importantly, economists noted that they would like to have central tendencies and distributions, rather than upper-bound estimates.

Although the discussants were in general agreement that there were benefits associated with reductions in air toxics emissions, they were split in their opinion about whether using the criteria pollutant model would work for air toxics. The case studies stimulated discussion about the advisability of pursuing a pollutant-by-pollutant, endpoint-by-endpoint evaluation of economic benefits.

The difficulties raised by the first two case studies were discussed. Namely, for the 188 listed HAPs, if we followed the criteria pollutant model, some difficulties would include: limited health effect data; difficulties in modeling multiple assaults on a target organ; contradictory or inconclusive evidence with respect to how many cases might develop or what organ would be targeted in humans; difficulties in extrapolation from animal models; uncertainties in extrapolating to lower doses; difficulties in evaluating background exposures (especially for national policy applications); and lack of resources to evaluate fully each chemical or class of chemicals listed in the Clean Air Act. The inability of economists to value relatively small risk reductions from endpoints whose biological significance is difficult to understand (e.g., change in platelet count) would hamper this approach even if the biological data base were complete and yielded best estimates and a characterization of variability. It was also discussed that the purpose of the workshop was to discuss one area (dose-response estimates) but that there are uncertainties in all of the other analytical steps (e.g., emissions, dispersion, exposure, and valuation). See Dr. Cameron's written comments (Appendix G) for a fuller explanation.

Possible alternatives to the criteria pollutant approach were also suggested. One suggestion was to evaluate "cleaning up the dirty stuff" or thinking of the HAP regulation as an insurance policy. Thus, economists would study the utility or value of peace-of-mind derived from knowing that the public was protected from the bundle of effects, either known or unknown, related to the listed HAPs. Another suggestion was to evaluate whether the public

held a different value for full elimination of an involuntary risk versus small incremental changes in that risk. A third promising possibility was to study the value of avoiding entry into a risk pool or shifts in the curve of population's onset of disease (e.g., as suggested in Dr. Weiss's paper). The Agency is considering introducing approaches similar to these proposals as alternatives to a damage-function approach for assessing benefits for control of criteria pollutants.

Although there was no consensus among the discussants, the research directions suggested by this workshop suggest a dual approach. The first avenue would involve continuing to address the HAPs using a damage function approach of estimating health effects avoided by a given policy and determining the economic value of avoided effects. The first two case studies (benzene and percholoroethlyene) lay out these issues very clearly. In addition, the comments by Dr. Cameron and Dr. Zeise provide insights and research suggestions.

The second research approach might involve some of the other ideas discussed at the workshop, including the concept of valuing the bundle of HAP reduction efforts embodied in the Clean Air Act from an economic perspective (i.e., the utility or value of peace-of-mind derived from knowing that the public was protected from the bundle of effects, either known or unknown, as opposed to the avoided health effects), the approach discussed in the manganese case study, and the insurance concept suggested in Dr. Smith's comments.

One of the invited discussants, Dr. Bailar, summarized the situation aptly by saying that benefit-cost analysis is an information-hungry process which we apply to an information-sparse problem with respect to HAPs. Regulatory decision-making informed by benefit-cost analysis is a precision-hungry process that at present we base on precision-sparse inputs. The workshop provided a meaningful first step, and more discussion and collaboration between the risk assessment and benefits assessment communities is needed.

APPENDIX A: LIST OF WORKSHOP PARTICIPANTS

CHAIR AND MODERATOR

Dr. Michael T. Kleinman, College of Medicine, University of California, Irvine, CA.

CO-MODERATOR

Dr. Roy Alpert, Division of Environmental Health, University of Cincinnati, Cincinnati, OH.

KEY DISCUSSANTS

Dr. John C. Bailar III, Department of Health Studies, University of Chicago, Chicago, IL.

Dr. Trudy Cameron, Department of Economics, University of California, Los Angeles, CA.

Ms. Lauraine Chestnut, Stratus Consulting, Boulder CO.

Dr. James Cogliano, Office of Research and Development, U.S. Environmental Protection Agency, Washington, D.C.

Dr. James DeMocker, Office of Air and Radiation, U.S. Environmental Protection Agency, Washington, D.C.

Dr. A. Myrick Freeman, Department of Economics, Bowdoin College, Brunswick, ME.

Dr. Paul Locke, Pew Environmental Health Commission, Baltimore, MD.

Dr. Albert McGartland, Office of Policy, Economics and Innovations, U.S. Environmental Protection Agency, Washington, D.C.

Dr. Dennis Paustenbach, Exponent, Menlo Park, CA.

Dr. V. Kerry Smith, Center for Environmental and Resource Economics Policy, Department of Agricultural and Resource Economics, North Carolina State University
Raleigh, NC.

Dr. Jeanette Wiltse, Office of Water, U.S. Environmental Protection Agency, Washington, D.C.

Dr. Lauren Zeise , California Environmental Protection Agency, Oakland, CA.

PRESENTERS OF WHITE PAPERS

Dr. Bernard Goldstein, Environmental and Occupational Health Sciences Institute, Robert Wood Johnson School of Medicine, Rutgers, Piscataway, NJ.

Dr. Lester Lave, Graduate School of Industrial Administration, Carnegie-Mellon University Pittsburgh, PA.

Dr. Lorenz Rhomberg, Gradient Corporation, Cambridge, MA.

Dr. Bernard Weiss, University of Rochester, Rochester, NY.

SAB STAFF

Dr. Angela Nugent, Science Advisory Board, U.S. Environmental Protection Agency, Washington, D.C.

APPENDIX B: AGENDA

SAB/EPA Workshop on the Benefits of Reductions in Exposure to Hazardous Air Pollutants: Developing Best Estimates of Dose-Response Functions

June 22-23, 2000
Westin Grand Hotel
West 2350 M Street, NW, Washington DC

Welcome, Brief Overview of Workshop, and Introductions	Michael Kleinman, University Of California, Irvine
9:15. **Background**	
Current approaches to Cancer and Noncancer Risk Assessment	William Farland, ORD
History of cost/benefit analysis for air pollution in general for Section 812 of the Clean Air Act Amendments	Albert McGartland, EPA James DeMocker, EPA
10:30 am **Review of Workshop Scope and Purpose**	Michael Kleinman
10:45 am **Economist's Perspective on HAP Benefits Analysis Under Section 812**	Lester Lave, Carnegie Mellon
11:15 am **Discussion of Morning Papers**	Michael Kleinman, Moderator, Key Discussants All Attendees
12:00 Noon **Lunch**	
1:00 pm **Case Study Presentations** (For each: 20 minute risk assessor presentation of issues, 30 minute core panel discussion, 30 minute general discussion [comments from all attendees])	Roy Albert, University of Cincinnati, Discussion Moderator
1:00 pm **Benzene**	Bernard Goldstein, EOHSI, Rutgers Key Discussants All Attendees
2:20 pm **Perclorethylene**	Lorenz Rhomberg, Gradient Corporation Key Discussants All Attendees

4:00 pm
Manganese — Bernard Weiss, University of Rochester
Key Discussants
All Attendees

5:20 pm **Adjourn**

June 23, 2000

9:00
Recap of Day 1 and Review of Workshop Agenda for Day 2 — Michael Kleinman

9:15
Discussion of Questions Before the Workshop — Roy Albert and Michael Kleinman, Moderators
Key Discussants
All Attendees

(1) Proposed approaches for hazard assessments for selected HAPs that would facilitate benefit assessments for those chemicals — Lead Discussants: Paul Locke, Laurie Chestnut

(2) Expert discussants' views on whether it is possible to produce a methodology for developing central tendencies and distributions in hazard assessments for HAPs for use in benefits analyses and how that might best be done — Lead Discussants: Dennis Paustenbach, Rick Freeman

(3) How best to identify limitations and uncertainties in both risk assessment methods and economic models — Lead Discussants: John Bailar, Kerry Smith

(4) Suggestions and priorities for a research agenda to address identified gaps in available data and methods needed to conduct HAPs related benefit analyses — Lead Discussants: Lauren Zeise, Trudy Cameron

11:30 am
Summary and Identification of Next Steps — Michael Kleinman, Moderator

12:00
Adjourn

APPENDIX C: WORKSHOP PROSPECTUS DISTRIBUTED BEFORE THE WORKSHOP

SAB/EPA Workshop on the Benefits of Reductions in Exposure to Hazardous Air Pollutants: Developing Best Estimates of Dose-Response Functions

Purpose

Hazardous air pollutants (HAPs) have been the focus of a number of EPA regulatory actions, which have resulted in significant reductions in emissions of HAPs. EPA has been unable to adequately assess the economic benefits associated with health improvements from these HAP reductions due to a lack of best estimate dose-response functions for health endpoints associated with exposure to HAPs and also due to the air quality and exposure models for HAPs available for use in benefits analysis. EPA is conducting two activities to develop a proposed methodology to generate estimates of the quantified and monetized benefits of reductions in exposure to HAPs. The first will be a workshop focusing on developing best estimates of dose-response functions that relate changes in HAP exposure to changes in health outcomes. The second activity will focus on (1) integrating these dose-response functions with appropriate models of HAP concentrations and human exposure and (2) translating these into economic benefits that would estimate changes in health risks resulting from regulations that reduce HAP emissions.

The overall goal of these two activities is to identify methods for the Agency to consider using in estimating changes in health risks resulting from HAP regulations that can be combined with valuation functions to estimate monetized benefits of HAP reductions.

Risk assessments for HAPs have been developed to help decision makers set health-based standards that are consistent with EPA's mission to protect human health. The quantitative toxicity values from these assessments (that is, the cancer slope factors and the noncancer reference concentrations and reference doses) are typically based on animal and epidemiologic studies that involve higher exposures than those encountered in the environment. The gap between environmental doses and study doses has led to toxicity values that can put a bound on the actual risk without being able to provide a reliable central estimate or distribution of risks. It is these latter terms (central estimates and distributions) that economists have traditionally used to estimate the economic value of potential changes in risks.

In contrast, risk assessments for criteria pollutants have been based on epidemiologic and clinical studies of exposures similar to those encountered in the environment. This has allowed development of standard statistical confidence intervals and distributions. With this information, economists have been able to develop economic benefit estimates for many health endpoints related to criteria pollutants. Criteria pollutant benefit estimates have been feasible

because of the availability of: (a) well-defined health endpoints such as hospital admissions or premature mortality; (b) dose-response functions from epidemiological and clinical studies which support estimates of risk reductions in terms amenable to economic valuation; (c) reliable estimates of ambient concentration and population exposure change; and (d) dose-response functions available from epidemiological and clinical studies in which the exposures were similar to those being experienced in the ambient environment. Uncertainties related to the health benefits of criteria pollutants have generally been represented by standard confidence intervals based on measures of within and between study variation in the estimated health effects.

While mortality from HAP-related cancer is a well-defined endpoint, there are very few validated exposure-response relationships. For the many other potential health effects from exposure to HAPs, such as changes in reproductive functions or mutagenic effects, there are major information gaps in all aspects of risk assessment, as well as in exposure-response and valuation. The focus of this workshop will be the development of best-estimates and uncertainty characterizations for hazard and dose response functions for use in benefits analyses of HAP regulations, with a focus on providing potentially useful data and tools to support HAP-related benefit assessments, including national-scale program evaluations.

Expected outcomes from this workshop will include a report documenting: (1) proposed approaches for hazard assessments for selected HAPs that would facilitate benefit assessments for those chemicals; (2) expert discussants' views on whether it is possible to produce a methodology for developing central tendencies and distributions in hazard assessments for HAPs for use in benefits analyses and how that might best be done; (3) h ow best to identify limitations and uncertainties in both risk assessment methods and economic models; and (4) suggestions and priorities for a research agenda to address identified gaps in available data and methods needed to conduct HAPs related benefit analyses.

Scope

The workshop will task expert discussants, who have knowledge and expertise in the fields of economics, health science, and risk assessment as related to managing HAPs, to address the following issues:

I. Whether it is possible to produce best estimates of the central tendencies and distributions of the dose-response functions for a set of well-defined health endpoints for each of the case-study HAPs for use in the second activity on air quality and exposure modeling and how that might best be done.

II. How best to identify limitations and uncertainties in both risk assessment methods and economic models with regards to changes in health risks from reductions in air toxic emissions, especially in the following areas:

A. Defining and characterizing best estimates and uncertainty distributions for hazard and dose response functions for both cancer and non-cancer effects.

B. Defining the context for the use of conservative reference doses, including the basis and methodology of the risk assessment.

C. Identifying potential uncertainties from extrapolating effects from "high dose" occupational and animal exposure studies to lower level ambient HAP concentrations.

D. Incorporating currently/typically available toxicity (both human and animal) data sets into existing or modified economic benefit models.

E. Evaluating the usefulness of benefits models based on dose-response functions derived from epidemiological studies as models for HAP benefit analyses.

III. Identifying gaps in existing knowledge and developing a proposed research agenda.

APPENDIX D: STRATEGIES FOR BRIDGING THE GAPS BETWEEN ECONOMISTS AND HEALTH SCIENTISTS

The Workshop resulted in many suggestions to address the gaps between economists and health scientists to improve benefits assessments for HAPs. These suggestions included the following:

1. Analyze the implications of current *in vivo* and *in vitro tests* for human toxicity for all known human carcinogens. Compare laboratory results with human data; for chemicals that are positive in the NTP bioassay, identify which are and which are unlikely to be human carcinogens. (Lave)

2. Invest time and resources in developing expert judgment on the best estimate for a chemical, like benzene, with substantial data on cancer and non-cancer effects and strong hazard identification but limited data at low doses. (Goldstein)

3. Acknowledge that data sets have major uncertainties. Invest in statistical approaches to characterize the distribution of uncertainties, even for chemicals with significant uncertainty in their data sets. Approaches would establish explicit weights for different assumptions associated with estimation of risk. Approaches would allow examination of the contribution to overall uncertainty from various components. (Rhomberg)

4. Link endpoints in toxicology studies to adverse effects the public cares about. Communicate these linkages and associated uncertainties to economists conducting benefit assessments. (Weiss)

5. Estimate economic value of avoiding entry into a risk pool or shifts in the curve of population's onset of disease. (Weiss)

6. Multiply the estimated number of cancer cases by a weighting factor that is determined by the strength of the evidence. (Albert)

7. Educate congress, the public, and the news media about "the art of the possible" in risk assessment and the limits of science. (Bailar)

8. Establish closer links between risk analysts and cost-benefit analysts. Establish cross-training programs. Establish regular, weekly meetings on each project in which risk analysis will be a significant element of a cost-benefit analysis. (Bailar)

9. Analyze the level of accuracy needed at each step of analysis to make most effective use of limited resources. (Bailar)

10. Consider "bundling" or grouping HAPs that are similar, either according to health endoint, chemical species, biologic mechanism or mode of action, or source categories. (Bailar)

11. Keep in mind that there were uncertainties not only in dose-response estimates that feed into cost-benefit analysis, but also in all of other analytical steps (e.g., emissions, dispersion, exposure, and valuation). (Cameron)

12. Consider a "top down" approach to benefits assessment, derived from individuals' subjective assessments of what HAP regulation would be likely to achieve in terms of health effects (or other effects) instead of aiming for "an unambiguous, objectively calculated, bottom-up measure" calculated on a chemical-by-chemical basis. (Cameron)

13. Develop a benefits assessment based on a "better understanding of the relationship between controls on emissions of HAPs and individuals' perceptions of safety or 'peace of mind.'"(Freeman, Lave, Smith)

14. Sort HAPs into "bins" according to the adverse effects of concern, and conduct benefit-cost analyses for different "bins." Distinguish chemicals listed due to their carcinogenicity, from chemicals listed because they are systemic (non-carcinogenic) toxicants, from irritants. For each group, develop a dose-response curve and build a distribution of points around the dose-response curve (for both carcinogens and non-carcinogens). (Paustenbach)

15. Invest in research to improve understanding and quantitative descriptions of how risk may vary in a population. This research would produce better mean estimates of risk and clearer understanding of the magnitude of risk borne by different individuals. (Zeise)